UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/627,207	07/25/2003	Cheng-Chi Lee	D6461	4237

7590 09/30/2004

Benjamin Aaron Adler
ADLER & ASSOCIATES
8011 Candle Lane
Houston, TX 77071

EXAMINER	
LIETO, LOUIS D	
ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 09/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/627,207	LEE ET AL.	
	Examiner	Art Unit	
	Louis D Lieto	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 August 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9* is/are pending in the application.

4a) Of the above claim(s) *1-4,8 and 9* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response to the Restriction was received on 8/19/2004. Claims 1-9 are pending in the instant application. Applicants elected the subject matter of group II, drawn to a method a method of diagnosing a neoplastic condition, and c-Myc as the species of circadian clock controlled gene, without traverse. Claims 1-4, 8 and 9 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a method of inhibiting tumor growth and a method of treatment of cancer. Claims 5-7 are currently under examination. It is noted that the claims have not been amended to reflect the elected subject matter. Applicant is reminded that the claims have only been examined to the extent that they read on the elected subject matter.

Priority

Priority to the provisional application U.S. No. 60/398,668 filed July 20, 2002 is acknowledged.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 5-7 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 5-7 continue to read on any circadian clock controlled gene. However, following Restriction/Election of species the claims have only been examined on a method of diagnosing a neoplastic condition in an individual based on the expression of c-Myc.

The specification does not reasonably provide enablement for a method of diagnosing any neoplastic condition based on any change in c-Myc expression. The term neoplastic condition is overly broad and includes conditions such as endometriosis, restenosis and cancer. The specification only discloses types of cancer, such as salivary gland hyperplasia, teratoma, lymphoma and angiosarcoma. The specification further fails to provide an enabling disclosure that correlates changes in c-Myc expression in any type of cell or tissue with the occurrence of any neoplastic condition. The specification teaches that after irradiation the level of c-Myc mRNA is higher in the livers of irradiated mPer2$^{m/m}$ mice than wildtype mice. The Per2 gene is a core circadian clock gene and mice with disruptions in this gene have been shown to spontaneously display salivary-gland hyperplasia and to develop spontaneous lymphoma {Fu et al. (2003) Nature Reviews 3:350-61; pg. 356, col. 1, pgph 4}. However the mPer2$^{m/m}$ mouse is not disclosed in the specification or known in the art to be a model for a particular type of cancer. There are no working examples that describe c-Myc levels in any tissues, other than the liver, in mPer2$^{m/m}$ mice. Additionally, the specification fails to disclose c-myc levels in non liver tissues or in any mammal suffering from a neoplastic disease. Further, the specification does not disclose that elevated c-Myc levels in the liver of mPer2$^{m/m}$ mice after irradiation are causative of, or correlate with the appearance of any type of cancer. Riegger et al. teaches that in 15 human cell lines the transcriptional rates of 2500 human genes were responsive to ionizing radiation {Riegger et al. (2004) Nucleic Acids Research 32:4786-4803; pg 4786, Abstract; pg. 4801, col.

1, pgph 2}. Specifically, c-Myc transcription was repressed after cellular exposure to ionizing radiation (Riegger et al., pg. 4790, Table 1). Thus, ionizing radiation has a broad effect on many genes, which has not been shown to specifically correlate with the induction of cancer.

While the specification discloses that c-Myc levels increase in irradiated livers of mPer2$^{m/m}$ mice, the specification does not correlate this change in c-Myc mRNA with tumorgenesis. The specification does not provide guidance on the stability of the c-Myc mRNA transcripts or on changes in the amount of c-Myc protein found in the mouse livers. Bernasconi et al. teaches that c-Myc protein is unstable and encoded by a very labile mRNA {Bernasconi et al. (2000) Am. J. Respir. Cell Mol. Boil. 23:560-565; pg. 560, col. 2, pgph 2}. Thus, it is difficult to correlate changes in c-Myc mRNA to changes in c-Myc protein levels without direct observation. The specification does not disclose a correlation of changes in c-Myc protein levels with changes in c-Myc mRNA levels in mPer2$^{m/m}$ mouse livers. Further, the specification teaches, "deregulation of c-Myc...alone does not result in neoplastic growth in mPer2$^{m/m}$ mouse livers" (Specification pg. 39, lines 5-8). Finally, the specification does not teach how an increase in c-Myc levels in the liver after irradiation of mPer2$^{m/m}$ mice correlates with the appearance of any neoplastic condition in the mPer2$^{m/m}$ mice. Given the teachings in the art that c-Myc mRNA levels decrease in cells after exposure to ionizing radiation, that the c-Myc protein is unstable, the teachings in the specification that only an increase in the level of c-Myc mRNA is detected in mPer2$^{m/m}$ mouse livers and the failure of the specification to correlate the level of c-Myc mRNA with the level of c-Myc protein, the skilled artisan would be would be unable to practice the invention as claimed without extensive and arduous experimentation.

The working examples do not disclose that any neoplastic condition was observed in the mouse livers after irradiation and concurrent with the increases in c-Myc levels. The specification does not teach that c-Myc expression changes in any other neoplastic condition, in mPer2$^{m/m}$ mice or other mammals. Mitas et al. teaches that c-Myc is not over expressed in lymph nodes containing metastatic breast cancer from humans {Mitas et al. (2001) Int. J. Cancer 93:162-171; pg. 166, col. 2}. Further, Woloschak et al. provides guidance that 70% of all pituitary tumors tested had c-Myc mRNA levels comparable to normal tissue {Woloschak et al. (1994) J. Clin. Endocrinol Metab. 79:253-7; pg. 256, col. 2, pgph 2}. Given the teachings in the art that correlating changes in c-Myc with a neoplastic condition is unpredictable, the teachings in the specification that deregulation of c-Myc levels does not cause the appearance of any neoplastic condition in mPer2$^{m/m}$ mice, the teachings that c-Myc levels only increase in mPer2$^{m/m}$ mouse livers after irradiation, and the lack of working examples in any other mammal or mouse strain, the skilled artisan would be unable to practice the invention as claimed without extensive and arduous experimentation.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 5-7 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 5 refers to a "light/dark cycle". The term "light/dark cycle" is vague and indefinite. Light/dark cycles could include a natural day/night of 24 hours or artificial cycles with shorter or loner durations. It is not clear from the body of the claim what constitutes a "light/dark cycle". As a result, the metes and bounds cannot be determined. Claims 6 and 7 depend on claim 5.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 5-7 are rejected under 35 U.S.C. 102(b) as being anticipated by Kononen et al. {Kononen et al. (1998) Nature Medicine 4:844-847}.

Kononen et al. teaches a method of diagnosing a neoplastic condition in an individual based on the changes in expression of c-Myc (Kononen et al., pg. 844, Abstract). Specifically, Kononen et al. provides guidance on the analysis of c-Myc expression in a tumor sample from an individual with breast cancer compared to a normal individual using tissue microarray technology (Kononen et al., pg. 844, col. 2, pgph 2; pg. 846, Methods). Further, Kononen et al. teaches that the tissue array technology can be used to diagnose new tumor sub-groups (Kononen et al., pg.845, col. 2, lines1-3). The term light/dark cycle is indefinite, see 112, 2nd paragraph rejection above, and has been interpreted to mean during any part of a normal day/night cycle. Thus, by teaching all the limitations of the claims as written, Kononen et al. anticipates the instant invention as claimed.

No claims free of the prior art of record

No claims allowed.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Lou Lieto whose telephone number is (571) 272-2932. The examiner can normally be reached on Monday-Friday, 9am-5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Amy J Nelson can be reached on (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is (703)-872-9306. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Patent applicants with problems or questions regarding electronic images that can be viewed in the PAIR can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Dr. Louis D. Lieto
Patent Examiner
Art Unit 1632

ANNE M. WEHBE' PH.D
PRIMARY EXAMINER